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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,421	08/29/2005	Norber Scharer	753-45 PCT/US	9129
23869 7590 11/19/2009 HOFFMANN & BARON, LLP 6900 JERICHO TURNPIKE SYOSSET, NY 11791				
EXAMINER				
CLARK, SARA E				
ART UNIT		PAPER NUMBER		
1612				
MAIL DATE		DELIVERY MODE		
11/19/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

10/521,421

Applicant(s)

SCHARER ET AL.

Examiner

SARA E. CLARK

Art Unit

1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

NON-FINAL REJECTION

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 5/18/2009.

Claims 1-3 and 8-21 have been amended and incorporate no new matter.

No new claims have been added.

Thus, claims 1-21 now represent all claims currently pending and under examination.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statements (IDS) have been submitted.

WITHDRAWN REJECTIONS

Rejections under 35 USC §112

In view of the amendments to claims 20 and 21, the rejection of claims 20 and 21 under 35 USC §112, second paragraph, for indefiniteness, has been withdrawn.

Rejections under 35 USC §103

Due to amendments to the claims, the rejection of **claims 1-3, 5-7, 9, 12-14, and 16-19** under 35 USC §103(a) as obvious over Bhattacharya et al. (EP 0298 652), King et al. (US Pat. 5,091,534) and Tsuji et al. (Tetrahed. Lett. 25(42), 4783-86, 1984) has been withdrawn.

Due to amendments to the claims, the rejection of **claims 1-4** under 35 USC §103(a) as obvious over Bhattacharya et al. (EP 0298 652), King et al. (US Pat.

5,091,534) and Tsuji et al. (Tetrahed. Lett. 25(42), 4783-86, 1984), further in view of Rasmusson et al. (US Pat. 4,760,071) has been withdrawn.

Due to amendments to the claims, the rejection of **claims 1, 8, and 11** under 35 USC §103(a) as obvious over Bhattacharya et al. (EP 0298 652), King et al. (US Pat. 5,091,534) and Tsuji et al. (Tetrahed. Lett. 25(42), 4783-86, 1984), further in view of Wakselman (*Encyc. Org. Reagents*, 2001) has been withdrawn.

Due to amendments to the claims, the rejection of **claims 1 and 10** under 35 USC §103(a) as obvious over Bhattacharya et al. (EP 0298 652), King et al. (US Pat. 5,091,534) and Tsuji et al. (Tetrahed. Lett. 25(42), 4783-86, 1984), further in view of King et al. (EP 0428366) has been withdrawn

Due to amendments to the claims, the rejection of **claim 15** under 35 USC §103(a) as obvious over Bhattacharya et al. (EP 0298 652), King et al. (US Pat. 5,091,534) and Tsuji et al. (Tetrahed. Lett. 25(42), 4783-86, 1984), further in view of Blaser et al. (US Pat. 4,335,054) has been withdrawn.

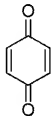
MAINTAINED REJECTIONS

The following rejections are maintained from the previous Office Action dated 2/18/2009, on the ground that the references cited therein continue to read on the limitations of the amended claims.

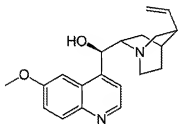
Rejections under 35 USC §112

Claim 11 stands rejected under 35 USC §112, second paragraph, for indefiniteness. Specifically, the amended claim recites the process of claim 1, characterized in that "in step (B) the compound of the general formula (II) for the introduction of the Boc protecting group has been reacted with Boc anhydride or Boc carbamate." However, the amendment inserting "in step (B)" is misleading, because step (A) is the protecting step, at which point Boc anhydride or Boc carbamate would be used to add the Boc protecting groups, while step (B) is the dehydrogenation (reduction) step, which takes place after the protecting groups have been added in step (A). The mixing of past and present tense ("for the introduction of the Boc protecting group" versus "has been reacted with") also creates a lack of clarity as to the point in time at which Boc anhydride or Boc carbamate are used to add the Boc protecting group. To avoid this uncertainty, suggested language for claim 11 is "the process of claim 1, characterized in that in step (A) the compound of the general formula (II) is reacted with Boc anhydride or Boc carbamate," which is how the claim shall be interpreted here.

Claim 16 stands rejected under 35 USC §112, second paragraph, for indefiniteness. Specifically, the amended claim recites the process of claim 1, characterized in that the **benzoquinone** used in step (B) is a substituted **quinine**, preferably a C₁₋₄ alkyl-, halogen-, cyano- or nitro-substituted **quinone**." As noted in the previous Office Action, claim 1 makes reference to a benzoquinone, not quinine. Benzoquinones are a class of compounds having the following core structure,



whereas quinine is a single compound of defined structure,



which does not belong to the class of benzoquinones. Therefore, Applicants' intent is unclear, such that claim 16 is insolubly ambiguous and cannot be interpreted in any meaningful way. See MPEP 2173.05(e).

NEW OBJECTIONS/REJECTIONS

1. Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

Specifically, amended claim 12 recites the process of claim 1, characterized in that "the dehydration catalyst in step (B) is selected from compounds of iron, ruthenium, and osmium; cobalt, rhodium, and iridium; nickel, palladium, and platinum; and copper, silver, and gold." However, claim 1 recites "a dehydrogenation catalyst selected from

compounds of group VIII of the periodic table of elements." Group VIII is older terminology which corresponds to the newer IUPAC terminology for groups 8 (iron, ruthenium, and osmium), 9 (cobalt, rhodium, and iridium), and 10 (nickel, palladium, and platinum). Group VIII does not include copper, silver, and gold, which belong to Group 11 (formerly Group IB) (see, for example, Fluck, Pure & App. Chem. 60(3) 431-436, 1988, p. 433). Therefore, claim 12 does not further limit the scope of claim 1.

2. Claim 19 is objected to because of the following informalities: "benzine," recited in the third line, is correctly spelled as "benzene." Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Regarding claims 2 and 16, the term "preferably" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

5. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 8 recites the process of claim 1, "characterized in that R₄ is alkoxycarbonyl, isobutyloxycarbonyl, tert-butyloxycarbonyl, tert-amtyloxycarbonyl, cyclobutyloxycarbonyl, 1-methylcyclobutyloxycarbonyl, cyclopentyloxycarbonyl, cyclohexyloxycarbonyl, and 1-methylcyclohexyloxycarbonyl."

Because R₄ cannot be all of these groups at once, claim 8 is interpreted as "R₄ is selected from the group consisting of" one of the recited functional groups.

6. Claim 12 recites the limitation "**dehydration** catalyst in step (B)" in the second line. There is insufficient antecedent basis for this limitation in the claim. Specifically, claim 1 recites a **dehydrogenation** catalyst in step (B), connoting the elimination of hydrogen atoms rather than a molecule of water. Clarification is requested.

7. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

Claim 18 recites the broad recitation "an alkali metal salt, an alkaline earth metal salt, an ammonium salt," and the claim also recites "a salt of sodium, potassium or ammonium," which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

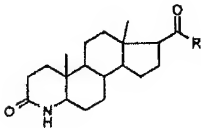
9. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain catalysts, does not reasonably provide enablement for all Group VIII metals as catalysts, as recited by claim 1, or for the Group VIII metals iron, ruthenium, osmium, cobalt, rhodium, iridium, nickel, palladium, and platinum, or for the Group IB metals copper, silver, and gold, as recited by claim 12. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

As recognized by MPEP 2164.01(a), "there are several factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." *In re Wands*, 8 USPQ2d 1400 (1988), sets out these factors, which include:

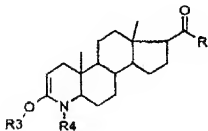
- (A)The breadth of the claims;
- (B)The nature of the invention;
- (C)The state of the prior art;
- (D)The level of one of ordinary skill;
- (E)The level of predictability in the art;
- (F)The amount of direction provided by the inventor;
- (G)The existence of working examples; and
- (H)The quantity of experimentation needed to make or use the invention.

The factors relevant to the present claims are analyzed below.

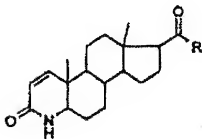
A. The Nature of the Invention. The claimed invention is a process for preparing a genus of steroidal compounds, starting with the reactant corresponding to general formula (II),



protecting the A-ring carbonyl oxygen and nitrogen hetero atom to yield an intermediate having the protecting groups R3 and R4, corresponding to general formula (III),



which is reacted with a dehydrogenation catalyst and an oxidizing agent to yield a product having a $C_1=C_2$ double bond, corresponding to general formula (I).



B. The Breadth of the Claims. By citing any catalyst selected from compounds of Group VIII of the periodic table, the scope of the claims goes well beyond the disclosure, encompassing reactions which have not been shown to be capable of being catalyzed by the full range of the catalysts claimed. In particular, claim 1 recites that the dehydrogenation catalyst is "selected from compounds of group VIII of the periodic table of elements, and claim 12 recites that the dehydration [sic] catalyst is selected from compounds of iron, ruthenium, and osmium; cobalt, rhodium, and iridium; nickel, palladium, and platinum; and copper, silver, and gold." None of these compounds have been demonstrated to promote the reaction of the claimed process, with the exception of certain palladium compounds (see, e.g., specification Examples 3 and 5, palladium acetate; Example 6, tris(dibenzylidene-acetone)-dipalladium-chloroform complex; and paras. 0039 and 0046, which refer generically to a palladium catalyst). The nature of the catalyst is essential to the reaction and the selection is critical. While the mechanism is not known with certainty, this is a homogenous catalysis and the substrate must intimately interact with the catalyst in an ordered fashion.

C. The State of the Prior Art and the Level of Predictability in the Art. The efficacy of a given catalyst in organic synthesis is unpredictable because it has not been established that all Group VIII compounds, or even all palladium compounds, would effectively catalyze the claimed reaction. For example, Ito et al. (J. Org. Chem. 43(5), pp. 1011-13, 1978) describe the regiospecific Pd(II)-catalyzed dehydrosilylation (protection followed by dehydrogenation and deprotection, as in the claimed invention) of silyl enol ethers, noting that PdCl_2 has been used to catalyze the direct dehydrogenation of saturated carbonyl compounds to give the corresponding α,β -unsaturated ketones, but generally in low yield. Instead, Ito et al. disclose the use of palladium acetate $\text{Pd}(\text{OAc})_2$ in acetonitrile, with p-benzoquinone to regenerate the catalyst, which was found to be much more effective. Even so, the product yield was heavily dependent upon the molar ratio of $\text{Pd}(\text{OAc})_2$ to benzoquinone (p. 1011, col. 1).

In addition, the selection of solvent can be as important as the selection of the catalyst and the molar ratios employed. For example, Minami et al. (Tetrahedron 42(11) 2971-77, 1986) disclose the efficacy of phosphine-free palladium catalysts in the preparation of α,β -unsaturated ketones and aldehydes in nitriles (specifically, a 1:1 molar ratio of $\text{Pd}(\text{OAc})_2$ and dppe in acetonitrile), noting that in other solvents such as THF or benzene, palladium black is deposited immediately and almost no reaction is observed (p. 2974, col. 1).

Tsuji et al. (Tetrahed. Lett. 25(42), pp. 4783-86, 1984, cited in the previous Office Action and on the IDS dated 4/25/2005) has proposed a mechanism for reactions utilizing combinations of a palladium dehydrogenation catalyst and an allylic carbonate

oxidizing agent. Palladium is peculiar in that it has the ability to readily shift between the 0 and +2 oxidation states, making complexes of palladium the only known catalysts for this reaction. Further, while claim 15 recites using 2,2'-bipyridyl or 1,10-phenanthroline to thermally stabilize the dehydrogenation catalyst, no evidence is provided that such an addition would stabilize the catalyst. Therefore, for these reasons, the state of the art must be regarded as highly unpredictable.

D. The Amount of Direction or Guidance Present and Presence or Absence of Working Examples. The only direction or guidance present in the specification is for the use of

- palladium acetate with benzoquinone in acetonitrile (Example 3);
- palladium acetate with allyl methyl carbonate in acetonitrile (Example 5);
- tris(dibenzylideneacetone)-dipalladium-chloroform complex with allyl methyl carbonate in acetonitrile (Example 6); and
- an unidentified palladium catalyst with allyl methyl carbonate in acetonitrile (Example 8, para. 0039; Example 9, para. 0046).

Therefore, the disclosure does not reasonably support the use of any Group VIII compound as the dehydrogenation catalyst of the claimed process, and provides no direction or instruction for the preparation of the claimed compounds employing catalysts other than those containing palladium.

E. The Quantity of Experimentation Needed and the Level of Skill in the Art. While the level of skill in organic synthesis arts is high, undue experimentation would be required for one of ordinary skill in the pertinent art to prepare the claimed compounds using any Group VIII catalyst, such that, without guidance or working examples in the specification, the claims lack enablement.

CONCLUSION

Claims 1-21 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARA E. CLARK/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612